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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/628,464

07/29/2003

Jon Elliot Adler

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EXAMINER

HOWARD, ZACHARY C

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/628,464	Applicant(s) ADLER ET AL.	
	Examiner Zachary C. Howard	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 November 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 118-123 and 128-141 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 118-120, 122, 123 and 128-140 is/are rejected.
- 7) ☒ Claim(s) 118, 120, 121 and 141 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment after final filed on 11/19/07 has been entered in full. Claims 124-127 are cancelled. Claims 118 and 120 are amended (Applicants indicate that these claims are "previously amended" but have made minor changes to the claims).

In view of Applicants' cancellation of claims 124-127, all rejections and/or objections to these claims that were maintained in the 10/22/07 Office Action are moot.

As such, the finality of the 7/18/07 Office Action is withdrawn. On further consideration, prosecution is re-opened in order to make several new rejections of record.

Claims 118-123 and 128-141 are under consideration.

New Objections and/or Rejections

Claim Objections

Claims 118 and 120 are objected to because of the following informalities:

(1) In claim 118, line 8, the word "[in]" has been introduced in the listing of claims filed 11/19/07 so that the claim recites: "...the nucleic acid sequence of [in] sequence...". It is noted that Applicants deleted the word "in" in the same location in the listing of claims filed 9/19/07 (indicated by a strikethrough, i.e. "~~in~~"). According to MPEP 714.II.C.B, double brackets, rather than single brackets, must be used to indicate deleted text in a claim. Therefore, claim 118 is now considered to be amended such that it includes the bracketed word "[in]". This bracketed word is objected to as being grammatically unnecessary.

(2) In claim 118, line 12, the words "operatively" and "linked" are missing a space between the words (i.e., they are written as "operativelylinked").

(3) In claim 120, line 3, the words "ligand" and "specifically" are missing a space between the words (i.e., they are written as "ligandspecifically").

Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 118-120, 122, 123, 128, 129 and 133-138 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO200257309 (Miwa et al, 7/25/02; cited previously) and further in view of U.S. Patent 5,763,218 (Fujii et al, 6/9/98; cited previously).

Claims 118-120, 122 and 123 each encompass an isolated nucleic acid sequence that encodes a polypeptide of SEQ ID NO: 2 and wherein said isolated nucleic acid sequence is operatively linked to a heterologous promoter that provides for the expression of thereof in a recombinant host cell. Claims 128 and 129 each depend from claim 118 and limit the promoter to an inducible or constitutive promoter. Claim 133 depends from claim 118 and limits the isolated nucleic acid molecule to one that further comprises a sequence that encodes a detectable marker. Claims 134-138 each encompass a HeLa human cell transfected with the nucleic acid sequence of claim 118.

Miwa teaches (pages 88-90) an amino acid sequence, SEQ ID NO: 1, that is encoded by the nucleic acid sequence SEQ ID NO: 2. The amino acid sequence of SEQ ID NO: 1 taught by Miwa is 100% identical to SEQ ID NO: 2 of the instant application. As indicated in the Abstract of Miwa, this sequence encodes a novel G-protein coupled receptor protein. Miwa et al further teaches (page 90) a 954 residue nucleic acid sequence (SEQ ID NO: 2) that is 99.6% similar to SEQ ID NO: 1 of the instant application. An alignment of these two nucleic acid sequences is attached to the 3/30/05 Office Action (see Attachment #1). SEQ ID NO: 1 of the instant application is 957 nucleotides in length. The sequence taught by Miwa is 954 nucleotides length and is missing the last 3 nucleotides as taught by SEQ ID NO: 1 of the instant application.

The alignment further indicates there is 1 conservative mismatch at position 930 of each sequence; at this position in SEQ ID NO: 1 of the instant application is a Y nucleotide residue, which indicates this position can be any pyrimidine (e.g. either a C or T), and Miwa at position 930 has a C. The Miwa publication is in Japanese and a full translation is not currently available to the Office; therefore, for purposes of prosecution it is assumed that the disclosure of Miwa does not teach the isolated nucleic acid operatively linked to a promoter, or host cells comprising said isolated nucleic acid.

Fujii teaches a nucleic acid encoding a novel human GPCR. Fujii further teaches "the nucleic acid sequence encoding the polypeptide of the present invention is under control of a suitable promoter" (col 14, lines 50-52). Fujii further teaches that the promoters include heterologous constitutive promoters such as the cytomegalovirus (CMV) promoter and heterologous inducible promoters such as the MMT promoter (col 14, lines 54-58). Fujii further teaches that the "polynucleotides of the present invention may also have the coding sequence fused in frame to a marker sequence..." (col 5, lines 27-30). Fujii further teaches "Various mammalian cell culture systems can also be employed to express recombinant protein... Examples of mammalian expression systems include the COS-7 lines of monkey kidney fibroblasts... and other cell lines capable of expressing a compatible vector, for example, the C127, 3T3, CHOHS293, HeLa and BHK cell lines" (column 10, lines 25-32). Therefore, Fujii teaches a system for heterologous expression of a novel GPCR in mammalian cell lines, including human cell lines.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to apply the heterologous expression systems as taught by Fujii to the novel GPCR encoded by SEQ ID NO: 2 as taught by Miwa. The person of ordinary skill in the art would be motivated to do so because Fujii teaches (in column 3) that the expressed GPCR protein can be used for further experimentation to screen for modulators of the GPCR function. The person of ordinary skill in the art would have expected success because Fujii teaches all of the techniques necessary to express a novel GPCR, and in the absence of other evidence, these techniques would be

expected to work as well with the novel GPCR taught by Miwa as with the novel GPCR taught by Fujii.

Claims 130-132, 139 and 140 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO200257309-A1 (Miwa et al, published July 25, 2002; cited previously) and further in view of U.S. Patent 5,763,218 (Fujii et al, published June 9, 1998; cited previously) and in further view of U.S. Patent 6,004,808 (Negulescu et al, published 12/21/1999; cited previously).

Claims 130-132, 139 and 140 each encompass an isolated recombinant HEK-293 host cell containing the isolated nucleic acid of claim 118 and that further express a sequence encoding a $G\alpha 15$ G protein (which is a promiscuous G-protein).

The teachings of Miwa and Fujii are summarized above. Neither Miwa nor Fujii teaches expression of a novel GPCR in a host cell further comprising a promiscuous G protein alpha subunit, such as $G\alpha 15$, or use of a host cell which is a HEK-293 cell.

Negulescu teaches "the invention provides ... a stable, isolated cell that expresses, from a construct, a $G\alpha$ subunit of a promiscuous G-protein (e.g., $G\alpha 15$ or $G\alpha 16$) ... these cells allow occupation of any G-protein coupled receptor (GPCR) by a ligand to be detected using a signal transduction detection system" (col 2, lines 14-25). Negulescu teaches "many embodiments of the invention will include a polynucleotide encoding a GPCR not naturally occurring in the cell and a promiscuous $G\alpha$ protein construct... The GPCR may be a GPCR of known function or of [sic] protein of unknown function, such as an orphan GPCR" (col 12, lines 17-36). Negulescu teaches that preferred host cells of the invention include HEK-293 cells (col 13, lines 42-43).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to apply the heterologous expression systems as taught by Fujii to the novel GPCR encoded by SEQ ID NO: 2 as taught by Miwa, and to use a HEK-293 host cell further comprising a $G\alpha 15$ subunit, such as $G\alpha 15$, as taught by Negulescu. The person of ordinary skill in the art would be motivated to do so because Miwa teaches a novel GPCR and Negulescu teaches that their method is applicable to any

GPCR of unknown function. The person of ordinary skill in the art would have expected success because Fujii and Negulescu teach all of the techniques necessary to express a novel GPCR with a G α 15 protein, and in the absence of other evidence, these techniques would be expected to work as well with the novel GPCR taught by Miwa as any other novel GPCR.

It is noted that cancelled claims in the application were previously rejected under 35 USC 102(a) as clearly anticipated by WO200257309-A1 (Miwa et al, published July 25, 2002). With respect to this rejection, the 2/15/07 Office Action stated:

"The rejection of claims 68-73 under 35 U.S.C. § 102(a) as being anticipated by WO200257309-A1 (Miwa et al, published July 25, 2002) set forth at pg 12-14 has not been applied to new claims 93-117 in view of the combination of (1) Applicants' submission on 12/6/06 of a 131 Affidavit executed by all of the inventors except for Elliot Adler; and (2) Applicants' 131 submission on 9/3/2005 of a 131 Affidavit executed by Robin Teskin; this Affidavit has been considered effective in place of an Affidavit executed by Elliot Adler in view of the Petition under 37 C.F.R 1.47(a) granted 3/11/2004. It is noted that MPEP 715.04 [R-5] states, "The following parties may make an affidavit or declaration under 37 CFR 1.131...(c) If a petition under 37 CFR 1.47 was granted ... the affidavit or declaration may be signed by the 37 CFR 1.47 applicant or the legal representative, where appropriate" (pg 3).

However, on further consideration the 1.131 Affidavits submitted by Applicants on 9/3/05 and 12/6/06 are not sufficient to overcome a rejection based on Miwa's 102(a) date (such as the instant 103(a) rejections set forth above) for the following reasons.

(1) One requirement of a declaration under 37 CFR 1.131 is that "[p]rior invention may not be established under this section in any country other than the United States, a NAFTA country, or a WTO member country. Prior invention may not be established under this section before December 8, 1993, in a NAFTA country other than the United States, or before January 1, 1996, in a WTO member country other than a NAFTA country." MPEP 715.07.III states, "The affidavit or declaration must state FACTS and produce such documentary evidence and exhibits in support thereof as are available to show conception and completion of invention in this country or in a NAFTA or WTO

member country (MPEP § 715.07(c)), at least the conception being at a date prior to the effective date of the reference." The signed Declarations submitted on 9/3/05 and 12/6/06 and do not meet these requirements, because they do not produce documentary evidence and exhibits showing conception and completion of invention in this country or in a NAFTA or WTO member country.

(2) The signed Declarations under 37 CFR 1.131 submitted by Applicants (9/3/05 and 12/6/06) are signed by less than all of the inventors of the claimed subject matter. The inventors listed on the Application are: Jon Adler, Alexey Pronin, Huixian Tang and Mark Zoller. As noted in the 2/15/07 Office Action, the legal representative for the 37 C.F.R. 1.47(a) Applicant (e.g., Robin Teskin) may sign a 1.131 declaration in place Jon Elliot Adler. However, while the 9/3/05 131 Declaration was signed by Robin Teskin, and the 12/6/06 131 Declaration was signed by Huixian Tang and Alexey Pronin, there is no 131 Declaration signed by Mark Zoller. It is noted that MPEP § 715.04 states, "where all of the named inventors of a pending application are not inventors of every claim of the application, any affidavit under 37 CFR 1.131 could be signed by only the inventor(s) of the subject matter of the rejected claims". See 37 CFR 131, which states: "An affidavit or declaration by less than all named inventors of an application is accepted where it is shown that less than all named inventors of an application invented the subject matter of the claim or claims under rejection. For example, one of two joint inventors is accepted where it is shown that one of the joint inventors is the sole inventor of the claim or claims under rejection." However, in the instant case, Applicants have not shown that Mark Zoller is not an inventor of the subject matter of the claim or claims under rejection. Applicants' comments accompanying the 131 Declarations filed on 9/3/05 and 12/6/06 do not indicate that Mark Zoller is not an inventor of the subject matter of the claim or claims under rejection. The 132 Declaration also filed on 12/6/06 appears to indicate that Mark Zoller is in fact an inventor of the claimed subject (nucleic acids encoding the hT2R76 of SEQ ID NO: 2).

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 128 and 129 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 128 and 129 each recite the limitation "operably linked" in line 2. There is insufficient antecedent basis for this limitation in the claim. Specifically, parent claim 118 uses the term "operatively linked" to indicate the linkage between the isolated nucleic acid and the heterologous promoter.

Conclusion

Claims 121 and 141 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

zch

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646